

WHAT IS CLAIMED IS:

1. An apparatus comprising:  
a semiconducting wafer;  
two electrical connectors adjacent to each other on the wafer, each of the connectors attached to the wafer at an attachment site with a gap disposed between the two attachment sites; and  
a power source connected to the wafer through the two electrical connectors.
2. The apparatus of claim 1 wherein the semiconducting wafer has a substantially rectangular shape with corresponding rectangular edges.
3. The apparatus of claim 2 wherein both attachment sites are near one of the edges.
4. The apparatus of claim 1 wherein the semiconducting wafer comprises a silicon wafer.
5. The apparatus of claim 4 wherein the semiconducting wafer comprises a doping agent.
6. The apparatus of claim 5 wherein the doping agent is selected from the group consisting of boron, phosphorous and arsenic.

7. The apparatus of claim 1 wherein the electric connectors and the power source are connected by electrical wires.

8. The apparatus of claim 7 further comprising control circuitry between the wafer and the power source.

9. The apparatus of claim 8 wherein the control circuitry comprises a temperature sensor disposed in the gap and electrically connected to a temperature controller.

10. The apparatus of claim 9 further comprising feedback control between the temperature sensor and the temperature controller to maintain the measurement of the temperature sensor within a selected range, and wherein the feedback control opens or closes a relay switch.

11. The apparatus of claim 8 wherein the control circuitry further comprises an electrical transformer connected in series between the power source and the electrical connectors.

12. The apparatus of claim 1 further comprising one or more stratum disposed on the wafer.

13. The apparatus of claim 12 wherein the stratum are selected from a group consisting of a DNA chip, a protein chip, a fluidic cell, a microscopic slide, liquid, coverslip, acrylamide gel and combinations thereof.

14. The apparatus of claim 12 further comprising samples disposed on the stratum.

15. The apparatus of claim 14 wherein the samples comprise molecules selected from the group consisting of nucleic acid molecules, polypeptides, carbohydrates, lipids, hormones, drugs and combinations thereof.

16. The apparatus of claim 14 further comprising labeled probes disposed on the stratum.

17. The apparatus of claim 16 wherein the labeled probes are selected from the group consisting of fluorescent labeled probes, chemiluminescent labeled probes and radiolabeled probes.

18. The apparatus of claim 12 further comprising members of a binding complex disposed on the stratum.

19. The apparatus of claim 1 wherein a temperature gradient formed on the wafer is

perpendicular to an attachment line derived from connecting the two attachment sites.

20. The apparatus of claim 1 wherein the wafer has clipped corners.

21. The apparatus of claim 1 wherein the two attachment sites are separated by a distance of between about 2 mm and about 180 mm.

22. The apparatus of claim 1 wherein the wafer comprises a substantially uniform composition.

23. A method of generating a temperature gradient comprising:

attaching two electrical connectors to a semiconducting wafer, wherein each of the connectors are adjacent to each other and attached to the wafer at an attachment site with a gap disposed between the attachment sites; and

connecting a power source to the wafer through the two electric connectors.

24. The method of claim 23 wherein the apparatus further comprises a temperature sensor attached at the same edge of the wafer as the electrical connectors and electrically connected to a temperature controller.

25. The method of claim 24 further comprising selecting a set point temperature on the temperature controller.

26. The method of claim 23 wherein the temperature gradient formed is substantially perpendicular to an attachment line connecting the two connectors.

27. The method of claim 26 wherein the temperature gradient formed is between about  $0.1^{\circ}\text{C}$  per millimeter and about  $1.0^{\circ}\text{C}$  per millimeter.

28. The method of claim 26 wherein the temperature gradient is between about  $0.25^{\circ}\text{C}$  per millimeter and about  $0.7^{\circ}\text{C}$  per millimeter.

29. The method of claim 23 wherein the wafer comprises silicon.

30. The method of claim 23 further comprising placing one or more stratum on the wafer to generate a temperature gradient on the stratum.

31. The method of claim 30 wherein the stratum comprise low thermal conductivity materials.

32. The method of claim 30 wherein the stratum are selected from the group consisting of microscopic

glass slides, fluidic cells, liquid, cover slips, acrylamide gel, DNA chips, protein chips and combinations thereof.

33. A method of analyzing biological macromolecules comprising:

establishing a temperature gradient on a semiconducting wafer having a stratum disposed thereupon, the stratum having one or more samples comprising biological macromolecules in thermal contact with the temperature gradient, the wafer having two electrical connectors connected to opposite poles of an electrical power source; and

evaluating the samples to determine thermal stability of complexes formed with the biological macromolecules in the samples wherein the samples are evaluated by measuring a property of the sample.

34. The method of claim 33 wherein the temperature gradient is substantially perpendicular to an attachment line derived from connecting the two electrical connectors.

35. The method of claim 33 wherein the biological macromolecules are nucleic acids.

36. The method of claim 35 wherein the stratum comprises a DNA chip with the nucleic acids.

37. The method of claim 35 wherein the stratum comprises an acrylamide gel having the nucleic acids.

38. The method of claim 35 wherein the evaluating comprises characterizing the thermal stabilities of nucleic acid molecules.

39. The method of claim 35 wherein the evaluating comprises characterizing the thermal stability of a complex formed by two single stranded nucleic acid molecules.

40. The method of claim 39 wherein the evaluating comprises characterizing the thermal stability of a complex formed by two single stranded nucleic acid molecules having one or more base mismatches.

41. The method of claim 36 wherein the evaluating comprises adding a labeled probe to the DNA chip, washing unbound labeled probe, detecting the activity of the labeled probe at various positions on the DNA chip and determining the thermal stability of the interaction between the labeled probe and the nucleic acid molecules on the chip by correlating the activity of the labeled probe with the temperature of the sample at the various positions on the DNA chip.

42. The method of claim 41 wherein the probe is a labeled nucleic acid.

43. The method of claim 42 wherein the correlating identifies the percentage of mismatch between the labeled nucleic acid probe and the nucleic acid molecules of the DNA chip.

44. The method of claim 35 wherein the evaluating comprises characterizing the thermal stabilities of nucleic acid hybrids formed with primers for use in polymerase chain reaction protocols.

45. The method of claim 33 wherein the biological macromolecules are polypeptides.

46. The method of claim 45 wherein the stratum is a glass chip.

47. The method of claim 45 wherein the polypeptides are selected from the group consisting of antigens, antibodies, enzymes, receptors and fragments thereof.

48. The method of claim 45 wherein the temperature gradient on the stratum is between about 20°C and about 45°C.

49. The method of claim 33 the evaluating comprises adding a labeled probe to the stratum.



50. The method of claim 49 wherein the evaluating comprises detecting the activity of the labeled probe at various positions on the temperature gradient and determining the stability of the interaction between the labeled probe and the biological macromolecule by correlating the activity of the labeled probe with the position on the temperature gradient.

51. The method of claim 49 wherein the label of the labeled probe is selected from the group consisting of fluorescent label, a radioactive label and a chemiluminescent label.

52. A method of conducting nucleic acid hybridization comprising:

establishing a temperature gradient on a stratum disposed on a semiconducting wafer, wherein one or more samples comprising nucleic acid molecules are disposed on the stratum that is in thermal contact with the temperature gradient, two electrical connectors being connected to the wafer and to opposite poles of an electrical power source; and

performing a hybridization protocol on the one or more samples to determine temperature effect based on the gradient.

53. The method of claim 52 wherein the stratum is selected from the group consisting of DNA chips and microscopic slides.

54. The method of claim 52 wherein the hybridization protocol comprises adding a labeled probe on the stratum.

55. The method of claim 52 wherein the method further comprises identifying the one or more samples that hybridized with the labeled probe.

56. The method of claim 52 wherein the hybridization protocol comprises conditions that can identify one or more base mismatches between the labeled probe and the unlabeled nucleic acid molecule.

57. The method of claim 52 wherein the wafer is substantially rectangular and comprises a plurality of edges, the two electrical connectors connected to the wafer at the same edge.

58. The method of claim 52 wherein the temperature gradient is substantially perpendicular to a line segment derived from connecting attachment sites of the two electrical connectors.

59. The method of claim 52 wherein the stratum comprises one or more equivalent samples in a row parallel to the temperature gradient.

60. A method of assessing binding complex interactions comprising:

establishing a temperature gradient on a semiconducting wafer having a stratum disposed thereupon, the stratum having one or more samples, each sample comprising one or more members of a binding complex in thermal contact with the temperature gradient, the wafer having two electrical connectors connected to opposite poles of an electrical power source; and

evaluating the samples to determine thermal stability of the binding complex on the stratum.

61. The method of claim 60 wherein the evaluating comprises adding a labeled probe to the stratum.

62. The method of claim 61 wherein one of the members of the binding complex comprises the labeled probe.

63. The method of claim 62 further comprising detecting the activity of the labeled member of the binding complex at various positions on the temperature gradient and determining the thermal stability of the

binding complex by correlating the activity of the labeled member with the position on the temperature gradient.

64. The method of claim 60 wherein the binding complex comprises a nucleic acid duplex.

65. The method of claim 60 wherein the binding complex comprises two or more polypeptides.

66. The method of claim 60 wherein the binding complex comprises a nucleic acid:polypeptide complex.

67. The method of claim 60 wherein the binding complex comprises a nucleic acid:drug complex.

68. The method of claim 60 wherein the binding complex comprises an antigen:antibody complex.

69. The method of claim 60 wherein the binding complex comprises a receptor:drug complex.

70. The method of claim 60 wherein the binding complex comprises a lipid:polypeptide complex.

71. The method of claim 60 wherein the binding complex comprises carbohydrate:polypeptide complex.

72. The method of claim 60 wherein the binding complex comprises a biological macromolecule and a binding partner of the biological macromolecule.

73. A method of generating a temperature gradient on a stratum comprising placing the stratum in thermal contact on a surface having a temperature gradient, the stratum having low thermal conductivity.

74. The method of claim 73 wherein the surface is a silicon wafer.

75. The method of claim 73 wherein the surface comprises aluminum blocks.

76. The method of claim 73 wherein the temperature gradient on the surface is generated by thermoelectric Peltier devices.

77. The method of claim 73 wherein the stratum comprises materials selected from the group consisting of glass, silicon and plastic.